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PREVALENCE OF FUNGAL KERATITIS IN RURAL POPULATION -AN INDIAN BASED PROSPECTIVE; RETROSPECTIVE STUDY

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ABSTRACT

Introduction: Fungal keratitis is a major eye disease leading to blindness in South Asia. Many authors has reported in South India, it was found that 44% of all central corneal ulcers are caused by fungi. This high prevalence of fungal pathogens in South India is significantly greater than that found in similar studies in Nepal (17%), Bangladesh (36%), Ghana (37.6%), and south Florida (35%). In Indian perspectives the incidence of fungal keratitis is being increased during the past decade, due to Intemperate and retrogressive climatic changes. The present study aims to find out the incidence of fungal keratitis in rural population.

Materials and Methods: A prospective and retrospective study of corneal ulcer conducted at Department of Ophthalmology, People Education Society Institute of Medical Sciences and Research, Kuppam, Andrapradesh, India. For accrual period of May 2010 to March 2011. Total of 100 patients were considered for the study with written consent and meet their inclusion criteria. A study details were documented with special reference to history of injury with vegetative matter, foreign body, use of antibiotics, steroids, plant juice, latex, milk, butter, etc. Concomitent clinical diagnostic history were tested with high specificity and sensitivity.

Results: Study revealed that the incidence of fungal keratitis was PPV (6.25) and the incidence rate was 0.625 with NPV -85.71%, specificity 17.24%, sensitivity 7.14%. Injury to the cornea is the leading cause of microbial keratitis, particularly fungal keratitis. Our study reported that, 36% of the patients had dry, moisture 50% and remaining patients had no evidence of both.

Conclusions: Fungal keratitis is responsible for a significant burden of blinding disease in the developing world. In winter season incidence is more and strongly associated with older age group population. Therapeutic gaps will probably persist, and further development is necessary. Basic awareness programme should be encapsulated and implemented by policy makers at rural areas.

KEYWORDS: PPV, Fungal Keratitis, NPV, Prevalence, Prospective

INTRODUCTION

The cornea assumes an unique place among all the body tissues due to its transparency, trivial diseases of the cornea can be disastrous to vision. WHO estimates globally 20-40 million are blind. In India approximately 10 millions of patients suffer from blindness, out of which 3.0 million are corneal blindness[1]. Total seventy fungus genera have been identified based on etiological agents in infectious keratitis[2]. The catastrophic organisms are brought by some contaminated foreign bodies like wooden piece, plant twig, thorn, food grain and husk. In this study site, many rural people practice agriculture and allied activities and they are more prone to fungal keratitis due to exposure of agriculture activities in open crop field without protection & awareness of diseases. Malnutrition, anemia, alcoholism and ignorance- predisposed

factors are influenced parameters for fungal infection and also other cohesive factors trigger the infection, namely use of steroids and broad-spectrum of antibiotics. Ophthalmologists have found that people are more prone to bacterial infections rather than fungal infections. Various fungal infection of the cornea poses a big problem and need special attention like therapeutic and their management options. The present study aims to know the incidence rate & clinical features among Keratitis and correlate response rate of antifungal therapy.

MATERIALS AND METHODS

A prospective study of corneal ulcer was conducted at People Education Society Institute of Medical Sciences and Research, Kuppam, Andrapradesh between May 2010-March2011. Total 100 inpatients and outpatients were considered for the study with written consent. All eligible patients meet their inclusion and exclusion criteria. A detailed history of the patients like past history of injury by vegetative matter, foreign body, use of antibiotics, steroids, plant juice, latex, milk, butter, etc. Secondary data were obtained from self structured questionnaires. Battery of examinations was done by five point scale; ocular examination was carried out using torch, magnifying glass and slit lamp examination. Ulcer, surface elevation or depression, dry or moist, edge-regular or frayed, satellite lesions, endothelial plaques, corneal sensation was carefully examined and documented systematically. KOH mount, gram stain and culture was developed by using standard laboratory procedures. Collected data was analyzed by using SPSS -19.50 versions. Chi-square goodness of fit, descriptive statistics like Mean, SD and 95% confidence interval was employed to draw the significant inference.

RESULTS: DEMOGRAPHIC PROFILE OF THE PATIENTS

The study comprises 51% males and 49% females, working age class was calculated between 29-35 yrs (9.0%), 36-40 yrs (7%), 37-46yrs (14.0%), 47-53yrs (44.0%), 54-59yrs (19.0%) and more than or equal to 60yrs were expressed (8%). The age group between 47-53 yrs were prone to fungal keritatis and statistically significant (P<0.05) with winter season. Occupation status was recorded during study period and it was found to be Agriculture (55.0%), Business (6.0%), House wife (25.0%), Labor(12.0%) and students were (2.0%). 97% of the patients belonging to rural areas practice agriculture and allied activities. Fungal corneal keratitis are affected in different season and it was expressed that in monsoon it was 47%, summer 29% and winter 24%. The mean interval between the onset of symptom and diagnosis was 2.6weeks (range: 1 – 9.3 weeks).

Table 1: Descriptive Statistics of Ulcer Patients

Sl.No	Age Class	N	Mean±SD	CI-95%	P-Value
01.	29-35 Years	09	32.44±2.29	30.04-35.69	P>0.05
02.	36-40 Years	07	37.71±1.49	35.81-39.26	P>0.05
03.	37-46 Years	14	44.07±1.49	40.01-46.82	P>0.05
04.	47-53 Years	44	51.20±1.69	49.88-53.63	P<0.05
05.	54-59 Years	19	56.05±1.71	54.63-58.00	P<0.05
06.	>=60 Years	08	59.62±0.74	56.28-60.33	P<0.05
	Total	**100**	**49.18±7.75**	**43.26-50.08**	

As per the study mean age of the patients was 49.88 ±7.75 years (CI 95%: 43.26 – 50.08). Different working class mean age was calculated based on ≤Mean±1/2 SD,1SD,2SD. Age class CI 29-35 years mean age was 32.44±2.29 yrs (CI 95% 30.04-35.69); 37.71±1.49 years (36-40years) CI 95% 35.81-39.26 years; 44.07±1.49 (37-46 Years) CI95% -40.01-46.82; 51.20±1.69years (47-53Years) CI95%-49.88-53.63; 56.05±1.71yrs (54-59 Years) CI95%- 54.63-58.00 and more than or equal to 60years mean age was59.62±0.74 years with CI-95% . 56.28-60.33 presented in Table (1).

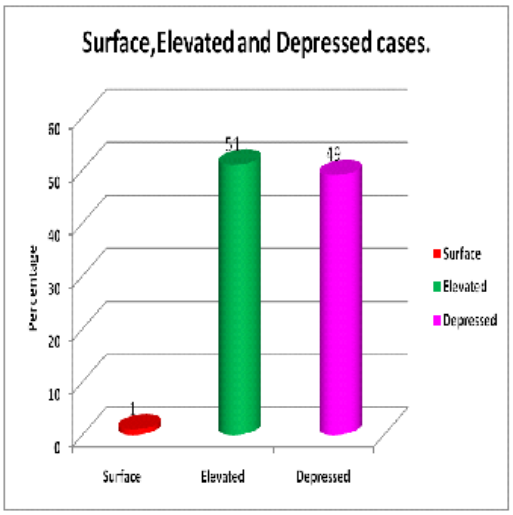

Figure (1a)

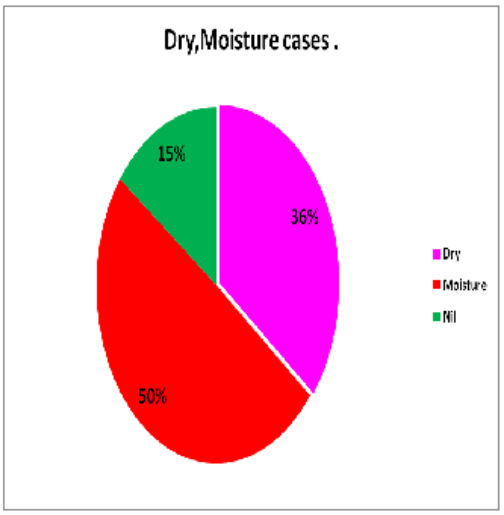

Figure (1b)

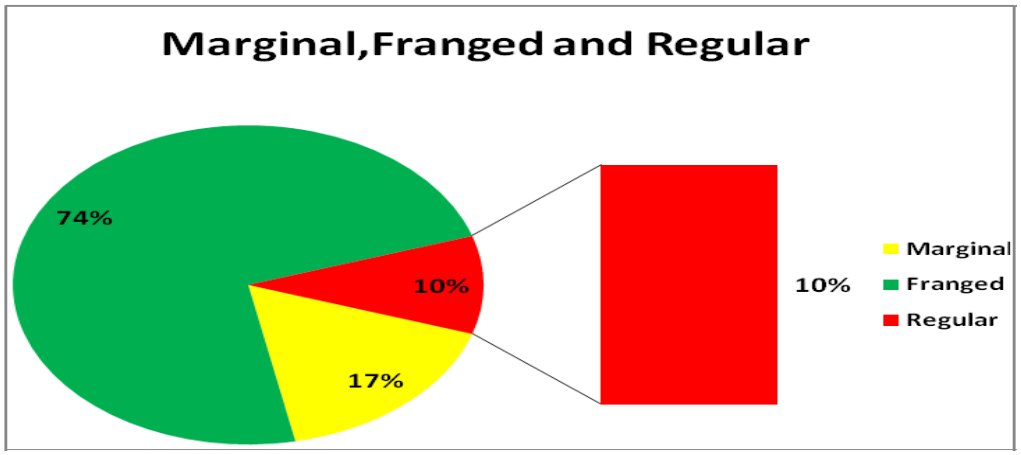

Figure (1c)

Surface (1), Elevated (51.0%) and depressed (49.0%) were noticed. The elevated and depressed cases were statistically significant with age of the person and occupation ($p<0.05$) Figure (1a). Matrix of careful examination of the study details clinically noticed dry (36.0%), Moisture (50.0%) and not affected was (15.0%).

Table 2: Incidence of FC-Types

Sl. No	Age Group	Fungal Culture		Total
		New Fungal Type Present	New Fungal Type Absent	
01.	29-40 years	01 (a)	15 (b)	(a+b) 16
02.	41-60 years	12 (c)	72 (d)	(c+d) 84
	Total	**(a+c)=13**	**(b+d)=87**	**100**

$$Positive\ predictive\ value(PPV) = \frac{a}{a+b}x100 \quad Negative\ predictive\ value(NPV) = \frac{d}{c+d}$$

$$Positive\ predictive\ value(PPV) = 6.25 \quad Negative\ predictive\ value(NPV) = 85.71$$

$$Specificity = \frac{d}{b+d}x100 \qquad Specificity = 17.24_{\%}$$

$$Specificity = \frac{15}{15+72} x100 \qquad Sensitivity = \frac{a}{a+c} x100$$

$$Sensitivity = \frac{1}{1+13} x100 \qquad Sensitivity = 7.14\%$$

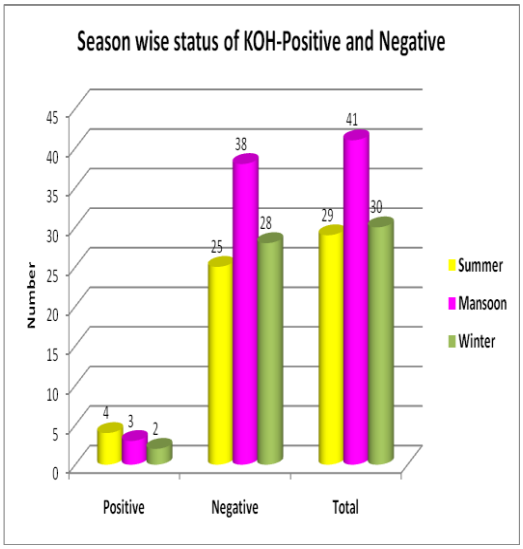

Figure (2a)

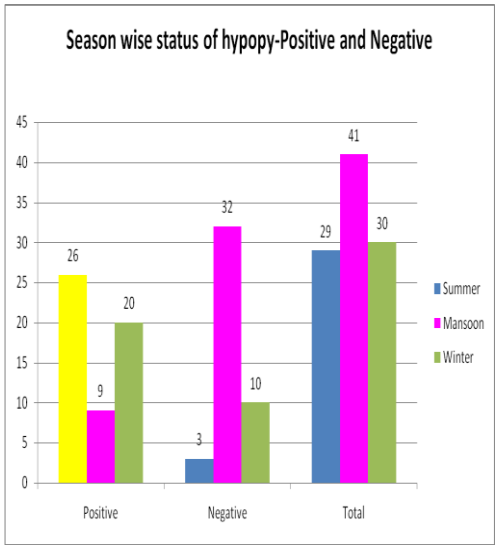

Figure (2b)

Fungal Culture

13% of ulcers yielded culture positive for fungal elements .87% were culture negative. among the positive cases. Fusarium (10)%, Aspergillus(2)% and cephalosporium(1)% were found

Predisposing Factors

Trauma with plant debris and straws were noted in two patients with fungal keratitis. Five patients received topical antibiotics. 25% patient had diabetes and another had local corneal disease (persistent corneal defect and stromal ulceration). 5% with fungal keratitis had a history of ocular surgery or use of contact lens and topical corticosteroid.77% patients previously used antibiotics 3% did not use antibiotics and rest of them were not responding.

Table 4: Signs Observed on Slit Lamp Examination of Patients with Fungal Keratitis

Sl	Signs	%	P-Value
01	Hypopyon	55(55.00%)	P<0.05
02	Feathery pattern	1(1.00%)	p>0.05
03	Satellite lesion	5(5.00%)	p>0.05
04	Conjunctival injection 3	03(3.00%)	p>0.05
05	Epithelial defect	04(4.00%)	p>0.05
06	Suppuration	04(4.00%)	p>0.05
07	Stromal infiltration	02(2.00%)	p>0.05
08	Anterior chamber reaction	01(1.00%)	p>0.05

Clinical Features

All patients had symptoms of redness and watering. Ocular pain and photophobia were found. 71.40 % of patients had foreign body sensation; 57.1% had decreased vision. The signs on slit lamp examination are shown in Table (4). Feathery pattern 1.00%, Satellite lesion (5.00%), Conjunctival injection 3.00%, Epithelial defect 4.00%, Suppuration 4.00%, Stromal infiltration 2.00% and Anterior chamber reaction 1.00%.

Table 5: Analysis of KOH and Season of Patients with Fungal Keratitis

Sl.No	Seasons	KOH		Total	Chi-Square Value
		+Ve	-Ve		
01	Summer	04	25	29	χ^2=6.82**. P Value≤0.05 With Degrees of freedom-2
02	Monsoon	03	38	41	
03	Winter	02	28	30	
	Total	**09**	**91**	**100**	

The analysis of KOH with different season were presented in Tab (5), KOH positives were 9.00% and they were statistically significant with seasons affected χ^2=6.82 (P Value≤0.05) with 2df. Analyses using KOH &season as the gold-standard test revealed sensitivities of 71.4% for KOH and 42.9% for season affected.

Figure 3: Diffuse Congestion, Scanty, Mucoid Discharge

Figure 4: Ciliary Congestion and Scanty Discharge

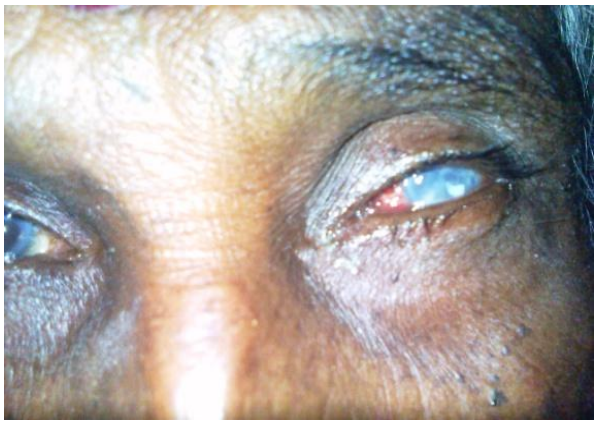

Figure 5: Diffuse Congestion and Scanty

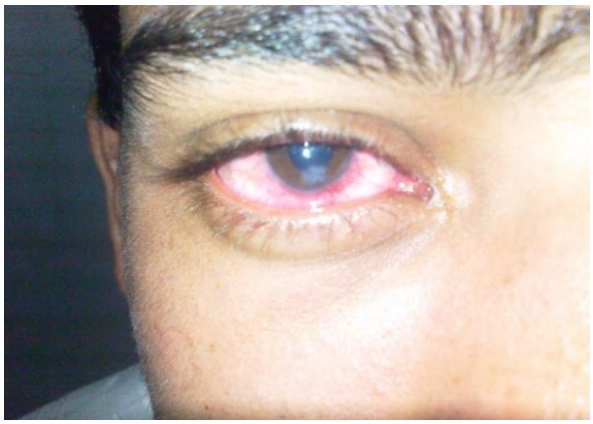

Figure 6: Corneal Oedema

DISCUSSIONS

Fungal keratitis is a major eye disease leading to blindness in Asia. One report from South India found that 44% of all central corneal ulcers are caused by fungi [2]. This high prevalence of fungal pathogens in South India is significantly greater than that found in similar studies in Nepal (17%), Bangladesh (36%), Ghana (37.6%), and south Florida (35%) [3–7]. In China, the incidence of fungal keratitis has increased during the past decade [8]. In temperate climates, such as Britain and the northern United States, the incidence of fungal keratitis remains very low [9, 10]. Our present study revealed that the incidence of fungal keratitis was PPV(6.25) and the incidence rate was 0.625 with NPV-85.71%, specificity 17.24%, sensitivity 7.14%. Injury to the cornea is the leading cause of microbial keratitis, particularly fungal keratitis. A history of corneal trauma with vegetative matter or organic matter is reported in 55 to 65% of fungal keratitis (11,12,13). A study from the northern United States reported trauma as the inciting event in only 8.3% of

cases [14]. In the southern United States, trauma was identified as a principal risk factor in 44% of children who had microbial keratitis and 27% among 227 cases of microbial keratitis reported in a non referral county practice in southern California [15, 16]. Several case reports published recently have identified contact lens wear as a risk factor for fungal keratitis in industrialized countries (29%) [17]. Patients wearing any type of contact lens can get fungal keratitis [18]. proposed study identified contact lens using patients were not affected by fungal corneal ulceration and it was statistically non significant (P>0.05).Many ophthalmologists identify topical steroids as the principal risk factor in enhancing ocular fungal growth. Steroid use as initial therapy was reported in 1 to 30% of patients having microbial keratitis [11, 12, 13,19]. However, several other large studies of infective keratitis reported from tropical countries do not support steroid use. Other factors were noticed like disorders, including corneal surface disorders, dry eye, bullous keratopathy, and exposure keratitis, are associated with the development of suppurative keratitis [14, 20]. Recently, several case reports of fungal keratitis after photorefractive keratectomy and Lasik have been published [18]. As for systemic factors, the incidence of fungal keratitis is not particularly high in immune compromised patients and those with diabetes [11).

The present study reported that, 36% of the patients had dry, moisture 50% and remaining patients had no evidence of both. During summer season patients will practice agriculture work in field without knowledge of protection of the eyes and they were infected by the plant debris and vegetative garbage.

The commonest etiologic agents were studied, filamentous fungi form the major etiologic agents of fungal keratitis. *Fusarium* species (10%), *Aspergillus* species (2.00%) and Cephalosporium (2.00%) have been implicated as main pathogens. Das et al., (25) reported that dematiaceous fungi are the cause of 8 to16.7% of cases of fungal keratitis [7, 11, 12, 19, and 24]. Most filamentous fungi associated with corneal ulceration in the tropics are found widely within the environment. Chang *et al.* [25] from Taiwan have reported that *Fusarium* species are common plant pathogens, particularly in corn crops or onion fields. Yeast can also cause keratitis. Gopinathan *et al.* [19] from India have reported *Candida* as a rare fungal corneal pathogen (0.7%). In a series of 24 patients from Wills Eye Hospital, Philadelphia, *Candida* was identified in 45.8% of cases of fungal keratitis; this probably represents the only study reporting *Candida* as the commonest etiologic agent of fungal keratitis [26].

Unlike the experience of bacterial keratitis, for the past two decades the spectrum of fungal pathogens causing fungal keratitis has not changed significantly[11]. yellowish white, and the base of the ulcer is often filled with soft, creamy, raised exudates, making it very easy to scrape the material even with a Kimura spatula. Feathery borders or hyphate edges are seen in 0% of patients, and satellite lesions in 10% of patients, with fungal keratitis (12) Hypopyon is present in 55% of cases [12]. Our study reported that fungal keratitis due to dematiaceous fungi is characterized by brown or black pigmentation on the surface of the ulcer, which appears dry, rough, and leathery; it can be difficult to obtain scrapings for culture using a spatula. An immune ring, satellite lesions, and posterior corneal abscess are seen frequently .Advanced *Fusarium* keratitis may progress to endophthalmitis.

Clinical Features

The working class age group 47-53 yrs were more affected with fungal keratitis and has been reported with large series of fungal ulcers and described dry, moisture, leathery, tough and raised surfaces**.** Bharathi *et al.* (12) reported a large series of fungal ulcers (1095) occurring in South India. In this study, Male patients were affected more commonly than female patients. Approximately 65% of patients were in the age group of 47to 53 years. For several decades, the fungal ulcer has been described as indolent and dry, with a leathery, tough, raised surface [12, 27, 28]. In this author's experience in treating several hundred fungal ulcers, the clinical features do not always correlate with classic textbook descriptions.

The Early fungal ulcer will appear like a dendritic ulcer of herpes simplex virus origin. The signs of inflammation will be minimal in comparison with bacterial keratitis. The absence of lid edema is a common feature. The infiltrates appear grayish-white or yellowish white.

Smear

Direct microscopic evaluation is the most valuable and rapid diagnostic tool for the detection of fungal filaments in corneal scrapings.Giemsa stain and Gram stain are equally sensitive in detecting fungal elements [30]. Thomas [28] has highlighted the sensitivity of various stains. Gram stain will identify fungal species in 45 to73% of cases, and Giemsa will identify fungi in 66%.Lactophenol cotton blue has a sensitivity of 70 to 80%,Grocott methylamine silver staining as much as 89% and calcofluor white of 80 to 90%. There have been differing reports on the sensitivity of the potassium hydroxide (KOH) smear. Proposed a retrospective study of 100 corneal ulcers reported that the sensitivity of the 10% KOH wet mount was higher (91.00%) than that of the Gram stained smear (88.73%) in the detection of fungal keratitis. Another study from South India reported equivalent sensitivities when 10% KOH smear (90%) was compared with calcofluor white (91%) (24).Conversely, Liesegang and Forster [7] and Forster and Rebell [31] have reported much lower sensitivities (5 to 33%) when using KOH. In our experience, 10% KOH wet mount is simple, cheap, rapid, and easy to interpret even by ophthalmic technicians. It is an ideal method for practice in tropical and developing countries.

Fungal Culture

Fungus grows within 48 to 72 hours in blood agar and Sabouraud dextrose agar kept at room temperature (27°C). The rate of positive culture in microbial keratitis ranges from 52 to 68% but depends on the severity of the ulcer and the criteria established for positive culture [5,12,,13]. The anterior chamber tap is extremely useful in the management of ocular infections confined to the anterior segment, deep keratitis, and posterior corneal abscess. The procedure should be performed under strict aseptic conditions.

CONCLUSIONS

Fungal keratitis is responsible for a significant burden of blinding disease in the developing world. In winter season incidence is more and strongly associated with older age group population. Therapeutic gaps will probably persist, and further development is necessary. In rural population fungal keratitis is very common, clinically suspected all fungal ulcers should be treated with antifungal agents irrespective of lab results. Priorities should be given to develop and undertake drug trials against fungal keratitis. Basic awareness programme should be encapsulated and implemented by policy makers at rural areas.

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